

REMARKS

Applicants acknowledge the time and courtesy extended by the Examiner, Mr. Hui, in conducting the Interview on July 22, 2009. The Examiner's Interview Summary thereof is noted. The amendments made above and remarks below provide applicants' summary of the interview.

The Amendments

Claim 57 is amended to change the vol% range for castor oil from 40-45% to 40-42%. Support for the claim amendment is found in the specification at page 8, line 30, to page 9, line 10, which recites ranges where endpoints at 40 and 45 vol% castor oil and/or 55% benzyl benzoate are explicitly recited. The disclosure of these ranges provides adequate support for recitation of the 40-42 vol% castor oil range. Although there is no explicit recitation of a 42 vol% castor oil value, the explicit support for the broader range of 40-45% provides adequate supports the narrower range of 40-42%. That a narrower range is implicitly described – sufficient for 35 U.S.C. §112 purposes – by explicit description of a broader range recitation finds direct legal support in the decisions of In re Wertheim, 191 USPQ 90, at 96 (CCPA 1976); and In re Voss, 194 USPQ 267, 271 (CCPA 1977). It is noted that Wertheim is favorably cited in the MPEP §2163.05(III) for this specific proposition. The facts in Wertheim and Voss which supported the decisions finding adequate support under 35 U.S.C. §112, first paragraph, are highly analogous to the instant facts. In Wertheim, a range recitation of 35-60% was found adequately supported by a disclosure which explicitly recited a range of 25-60% but contained no range with a 35% endpoint or example with a 35% value. In Voss (at 272, n. 14) the court indicated that a description of a broad range, i.e. 20-100%, "would necessarily describe" a range

contained within the broader range, i.e. 50-100%. In accordance with the law, therefore, applicants urge that amended claim 57 is adequately described by the original specification under 35 U.S.C. §112, first paragraph.

Previous claim 59 is rewritten in independent form as new claim 68. Support for this claim is also found in the specification at page 8, line 30, to page 9, line 10, which includes a recitation of the 40% castor oil value and also includes recitation of the “about” term in connection with the percentage amount of the cosolvent. One of ordinary skill in the art would clearly recognize that, in addition to the 40% value, applicants possessed the invention where the value is “about 40 vol%.” The new dependent claims from claim 68 mirror the previously existing dependent claims from claim 57.

Applicants reserve the right to file one or more continuing and/or divisional applications directed to any subject matter disclosed in the application which has been canceled by any of the above amendments.

The Rejection under 35 U.S.C. §112, first paragraph

The rejection of claim 65 under 35 U.S.C. §112, first paragraph, is respectfully traversed. The recitation that the “composition contains no plant oil other than castor oil” finds essentially literal support in the specification at page 8, lines 36-38. Thus, the rejection should be withdrawn.

The Rejection under 35 U.S.C. §103

The rejection of claims 57-60 and 63-67 under 35 U.S.C. §103, as being obvious over

WO 95/12383 in view of Riffkin (J.Pharm.Sci. 1964), is respectfully traversed.

As discussed in the Interview and established in the prior prosecution, the remaining issue is whether the data applicants have provided by way of 37 C.F.R. §1.132 declarations provides a showing of nonobviousness which is representative of the unexpected advantages of the current claims and commensurate in scope with the claims. The previous prosecution shows that the Examiner agrees that the results demonstrate a significant advantage for the embodiment within the claimed scope over the embodiments encompassed by the prior art. However, the Examiner did not agree that the showing for an embodiment within the claims having 40.7 vol% castor oil (“CO”) was commensurate in scope to show nonobviousness for claims reciting 40-45 vol% CO when the prior art (Riffkin) contained an embodiment of 50% CO.

Currently, two independent claims are presented, one reciting 40-42 vol% CO and one reciting about 40 vol% CO. Applicants urge that there should now be no question that the showing at 40.7 vol% is reasonably representative of and commensurate in scope with the current claims. See, e.g., In re Kollman, 201 USPQ 193 (CCPA 1979); In re Clemens, 622 F.2d 1029, 1036, 206 USPQ 289, 296 (CCPA 1980); and MPEP §2145; regarding the reasonably representative standard of review.

Another outstanding issue was what exactly is disclosed in Riffkin’s embodiments reciting a % value for the CO and BB content because the reference does not explicitly indicate whether this % value is by weight or by volume. On this issue, applicants file herewith a further Declaration under 37 C.F.R. §1.132 of Dr. Fricke. For the several reasons stated in the Declaration, Dr. Fricke concludes that the only practical interpretation of the Riffkin et al. disclosure is that the % values given in the Tables refer to the percent by weight. Thus, for

example, the 50% CO/50% BB vehicle described in Riffkin's Table IV is, in fact, describing a composition which contains 53.9 vol% of CO when converted from the 50 weight% value.

Additionally, although for the above reasons applicants' position is that Riffkin must refer to weight% for its values, a further experiment is provided in the attached 37 C.F.R. §1.132 declaration comparing a 50 vol% castor oil/50 vol% benzyl benzoate vehicle embodiment under the same protocol as the experiments in Dr. Fricke's previous declaration. The results confirm the advantage of the claimed invention over Riffkin even if it can be interpreted to be in vol%.

For completeness of the record, applicants provide the following rephrasing of the nature of the showing of nonobviousness in view of the current claims and the clarification of the Riffkin reference, as discussed above.

The data of record provides a side-by-side comparison of the stability of a composition representative of the claimed invention with compositions where the vehicle is otherwise the same but having higher amounts of castor oil, such as taught by Riffkin (as discussed further below, the steroid used in the Riffkin compositions is not testosterone undecanoate). Multiple ampoules of compositions containing testosterone undecanoate, benzyl benzoate and castor oil were tested side-by-side for stability (lack of precipitate crystals) over 34 days. One set of ampoules contained 60 weight% castor oil (i.e., 63.7 vol%), one set 50 weight% (i.e., 53.9 vol%), one set 50 vol% and one set 37 weight% (i.e., 40.7 vol%). All of the ampoules which contained 37 weight% castor oil (i.e., 40.7 vol%) – thus being representative of the claimed invention – maintained stability with no precipitate for the full 34 days. For the compositions which contained 50 vol%, 50 weight% (i.e., 53.9 vol%) and 60% weight% (i.e., 63.7 vol%) castor oil, most of the ampoules lost stability before 34 days.

The advantage in stability of the compositions, when using a lower amount of castor oil as recited in the instant claims, could not have been expected from the prior art. Neither reference teaches any advantage in stability for its compositions based on the proportions of the vehicle components, or otherwise. Further, to the extent Riffkin suggests to use castor oil in the WO '383 compositions, it fails to teach or suggest amounts as low as in the recited claims. The lowest amount of CO in a vehicle used together with a steroid taught by Riffkin is 52 weight% (see Tables V and VI) and the CO amounts range up to 80 weight%. This lowest amount converts to 56.0 vol% CO. Riffkin also presents a 50/50 weight% mixture of CO and BB in Table IV but not mixed with a steroid. This converts to 53.9 vol.% CO. The comparison provided in the declaration shows the advantage of the claimed compositions over compositions containing 53.9 vol% CO (as well as over compositions containing 50 vol% CO). Thus, in terms of CO content, the comparison is made either to the exact closest embodiment of Riffkin or an embodiment which is even closer to the claimed invention than the closest embodiment of Riffkin (depending on whether the steroid must be present to be consider the closest embodiment and whether the % values are by volume or weight). In either event, the unexpected advantage in stability of the solutions according to applicants' invention using a lower amount of castor oil over the prior art teachings using a higher amount has clearly and convincingly been demonstrated.

Applicants' declaration also provides data comparing the stability of solutions containing castor oil compared to peanut oil and miglyol solutions which further bolster the case for nonobviousness. These comparisons clearly show that castor oil is advantageous over these other oils. Thus, the comparison also shows the advantage in stability of the solutions of the

claimed invention using castor oil over those having the first-listed preferred oil of WO '383, i.e., peanut oil.

The above-discussed advantages discovered by applicants were discussed in applicants' specification (page 10, lines 24-33):

The compositions of the invention are chemically stable with respect to the testosterone esters. That is to say that degradation products could not be detected after long term storage (such as after 7 weeks or 17 weeks or even longer) at conditions normally known to accelerate degradation processes, such as variations in temperatures, high and low temperatures and various relative humidity. For example, less than 1% by weight of degradation products of testosterone esters is present after storage of the composition for at least 7 weeks, such as for 16 or 17 weeks, for 6 months, or for 9 or 12 months at 40 °C and 25 % RH in darkness. Preferably, less than 0.5 % w/w, such as less than 0.2 % w/w of degradation products of testosterone esters is present after storage at the above-mentioned conditions.

The references do not teach or suggest anything regarding such advantageous stability properties. Thus, the advantages are clearly unexpected from the prior art and provide a clear and convincing case for nonobviousness. For all of the above reasons, it is urged that the data of record as a whole provides clear and convincing proof of the unexpected advantages of the claimed invention and thus the nonobviousness of the claimed invention.

Applicants further submit that the references fail to support a prima facie case of obviousness in the first instance or, alternatively, that any such case is a weak one which makes the showing of nonobviousness even more convincing.

WO '383 discloses an injectable solution of testosterone undecanoate with an injectable plant oil and/or benzyl benzoate. WO '383 provides no suggestion to use castor oil as the plant oil in its compositions. To the contrary, at page 4 of the publication, WO '383 recites the

possible use of peanut, soy, sesame, tea or olive oils. WO '383 also provides no suggestion as to the relative amounts of the plant oil and benzyl benzoate. Particularly, there is no suggestion of a composition of testosterone undecanoate contained in a vehicle comprising castor oil and benzyl benzoate where the castor oil is in a concentration of 40 to 42% by volume or about 40% by volume in the vehicle, as recited in the current claims.

The Office action alleges that it would have been obvious to one of ordinary skill in the art to modify the teachings of WO '383 in view of Riffkin since Riffkin teaches the use of a vehicle having castor oil and benzyl benzoate in defined relative amounts for delivering steroidal compositions parenterally. Riffkin discusses the use a combination of castor oil and benzyl benzoate as a vehicle for steroid hormones generally. However, Riffkin discloses no such combination of a vehicle with a testosterone ester. Riffkin discloses 5 examples of vehicles with castor oil and benzyl benzoate without a steroid in Table IV, page 893, and 6 examples of vehicles with castor oil and benzyl benzoate containing a steroid in Tables V and VI, page 894. In the vehicles where a steroid is contained, the amount of castor oil ranges from 52 to 80 weight%, i.e., well above the maximum values recited in the instant claims.

Applicants respectfully submit that one of ordinary skill in the art would not have been motivated or otherwise had a reason to modify the compositions of WO '383 in view of Riffkin to provide a composition meeting the requirements of the instant claims. If one of ordinary skill in the art were to modify the WO '383 compositions in view of Riffkin, they would use castor oil as the plant oil in an amount of 52-80 weight% – which converts to even higher values of % by volume – in the composition according to Riffkin's teachings. Such a composition would not meet the recitations of the instant claims, i.e., a vehicle comprising castor oil in a concentration

of 40 to 42% by volume or about 40% by volume. There are no other suggestions from the cited references to provide a composition, as claimed, having this amount of castor oil.

It was alleged in the previous Final office action that “optimization of the amount of excipients is considered obvious as being within the purview of the skilled artisan.” However, there is no factual basis on the record to support that lowering the amount of castor oil would result in optimization – or what property would be optimized. In order to support obviousness to modify an amount of a component in a composition for purposes of optimization, there must be some basis provided on the record that the modification of the amount would optimize some aspect of the composition. There is no basis to assert such here. The Office action merely alleges optimization but indicates no objective – based on the references’ teachings – for such optimization or what aspect is intended to be optimized. Further, no reference of record provides any support that lowering the castor oil amount would optimize the composition in any way. To the contrary, the only teachings of record regarding an amount of castor oil come from Riffkin which teaches 50 or 52 weight% CO as a minimum and up to 80 weight% CO. Since Riffkin clearly pointed one of ordinary skilled in the art to this amount range, the only reasonable conclusion such skilled artisan could draw from the record here is that 50 or 52 weight% – as a minimum – up to 80% is the optimal range and other amounts would, therefore, be less than optimal. There is certainly no direction from the cited prior art that lowering the amount of castor oil would lead to optimization or what property would be optimized. The only suggestion of this comes from applicants’ own teachings and data.

Additionally, no basis in the law is cited for the proposition that “optimization of the amount of excipients is considered obvious as being within the purview of the skilled artisan.”

The context of the statement in the Office action and the failure of any factual support for it, leaves the impression that it is allegedly per se obvious to modify the amounts of a reference composition to achieve some undefined “optimization.” If this is what is being alleged, it is clearly contrary to the law. Lacking any evidentiary support, the alleged general optimization argument is merely a conclusory statement of the type the Supreme Court recently cautioned against using to support an obviousness rejection; see, KSR International Co. v. Teleflex Inc., 550 U.S. ___, 82 USPQ2d 1385, at 1396 (2007), stating: “rejections on obviousness cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness.” A general statement that some undefined optimization would be obvious is not a sufficient rational underpinning to support the rejection.

For all of the above reasons, it is urged as a separate basis for patentability that the cited references fail to establish a prima facie case for obviousness. Thus, the rejection under 35 U.S.C. §103 should be withdrawn for this additional reason.

For all of the above reasons, it is urged that the combined teachings of WO ‘383 in view of Riffkin, particularly when considered in light of the declaration evidence of nonobviousness, fail to render the claimed invention obvious to one of ordinary skill in the art. Thus, the rejection under 35 U.S.C. §103 should be withdrawn.

It is believed that the claims are in condition for allowance. However, the examiner is kindly invited to contact the undersigned by telephone to discuss matters which may further the prosecution of this application or facilitate the allowability of some or all of the claims herein.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,

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